QUIZ NAVIGATION

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Grade	9.00 out of 10.00 (90%)

Question 1

ID: 50274

Correct

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JM is a 24-year-old male who was recently diagnosed with Major Depressive Disorder (MDD). He has no known allergies and no other medications or medical conditions. The symptoms that JM has reported include the following:

- **Having a depressed mood and feeling "hopeless", almost every day**
- **Feeling fatigued at all times of the day, almost every day**
- **Loss of desire for previous interests (i.e. socializing with friends, playing soccer)**

He agrees to start a trial on fluoxetine 10 mg PO daily which will be titrated up to an optimal dose.

What is the earliest time frame to assess the efficacy of a therapeutic dose of an antidepressant?

Select one:

a. 1 week ✖

b. 3 to 4 months ✖

c. 2 to 4 weeks ✔

Rose Wang (ID:113212) this answer is correct. An early response can be assessed after 2 to 4 weeks of taking the target dose of medication.

d. 8 to 12 weeks ✖

Correct

Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Determine the earliest time frame to assess the efficacy of an antidepressant.

BACKGROUND:

Major Depressive Disorder (MDD) is a mental health disorder characterized by a state of low/depressed mood which impacts an individual's emotional, physical, cognitive, and behavioural well-being. MDD is diagnosed using the DSM-5 criteria which identify symptoms such as appetite changes, sleep changes, depressed mood, loss of pleasure and their impact on a person's functionality. Non-pharmacologic and pharmacologic therapy is the mainstay of treatment. Various antidepressants have been developed and tested to treat MDD. Different classes have different side effect profiles, and drug interaction profiles. Generally speaking, first-line options are tried first based on patient characteristics (comorbidities, drug interactions, cost etc.). Once treatment is started, patients should be monitored for side effects of the antidepressant, improvement in their emotional, and physical symptoms, and improvement in their functionality. These parameters need to be measured at different times because the drugs often affect each category differently. When monitoring for tolerability, side effects can be realized within 1-2 weeks. Early improvement of physical symptoms (e.g. sleep and appetite changes) can occur within 2-4 weeks while cognitive and emotional symptoms take longer to show improvement (around 4-6 weeks). The full effect of treatment may take up to 8-12 weeks to demonstrate its efficacy.

RATIONALE:

Correct Answer:

- **2 to 4 weeks** - An early response can be assessed after 2-4 weeks of taking the target dose of medication.

Incorrect Answers:

- **1 week** - This is too short of a time frame to see a response in efficacy.
- **3 to 4 months** - This is not the earliest time frame to assess efficacy.
- **8 to 12 weeks** - This is not the earliest time frame to assess efficacy.

TAKEAWAY/KEY POINTS:

The earliest clinicians can assess the efficacy of drug therapy is 2-4 weeks after therapeutic doses have been reached.

REFERENCE:

[1] Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments. *Can J Psychiatry*. 2016;61(9):540-560. doi:10.1177/0706743716659417.
[2] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.

The correct answer is: 2 to 4 weeks

Question 2
ID: 50275
Correct
Flag question
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You are a hospital pharmacist responsible for conducting an educational in-service session for the staff on the inpatient mental health ward. During the session, you emphasize the importance of understanding various aspects of antidepressant therapy, including discontinuation and tapering.

Which one of the following Selective Serotonin Reuptake Inhibitors (SSRIs) would you instruct the staff can be tapered most rapidly?

Select one:

a. Paroxetine ✖
b. Sertraline ✖
c. Fluoxetine ✔
d. Citalopram ✖

Rose Wang (ID:113212) this answer is correct. Fluoxetine can be tapered the fastest out of these options, due to its long half-life.

Correct
Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Identify which Selective Serotonin Reuptake Inhibitor (SSRI) has the longest half-life. Understand the relationship between half-life and tapering.

BACKGROUND:

Side effects of SSRIs include insomnia (especially fluoxetine and sertraline which are more activating) or drowsiness, sexual dysfunction and gastrointestinal (GI) upset. The CNS and GI side effects normally subside within 2 weeks; however, sexual dysfunction could persist for the duration of treatment. Additionally, when initiating an SSRI or increasing the dose, anxiety and agitation are common side effects that may occur; however, they usually subside within a few weeks. SSRIs can increase the risk of GI bleeding and should be used with caution in individuals at higher risk of GI bleeding (such as concomitant NSAID use). In addition, fluoxetine has a uniquely long half-life of 4-6 days (9 days for active metabolite norfluoxetine), allowing for faster tapering upon discontinuation compared to other SSRIs. A meta-analysis comparing escitalopram to citalopram found that escitalopram, the stereoisomer of citalopram, was superior in efficacy, but comparable in adverse events to citalopram. Both citalopram and escitalopram carry the greatest risk amongst the SSRIs of prolongation of QTc. In addition, paroxetine has the greatest anticholinergic effects and causes the greatest amount of weight gain among the SSRI drug class. Withdrawal symptoms can be described by the FINISH mnemonic and include flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal. These unpleasant, but non life-threatening symptoms may be experienced by up to 40% of patients when antidepressants are stopped abruptly. Therefore, when discontinuing antidepressants, taper slowly over 4 to 6 weeks to prevent withdrawal symptoms. Patients are at risk if they have been using the antidepressants for a minimum of 6 weeks. Paroxetine and venlafaxine are the most likely to be associated with discontinuation symptoms; whereas, fluoxetine and vortioxetine cause little to no withdrawal symptoms.

RATIONALE:

Correct Answer:

- **Fluoxetine** - Fluoxetine can be tapered the fastest out of these options, due to its long half-life.

Incorrect Answers:

- **Paroxetine** - Paroxetine cannot be tapered the fastest out of these options.
- **Sertraline** - Sertraline cannot be tapered the fastest out of these options.
- **Citalopram** - Citalopram cannot be tapered the fastest out of these options.

TAKEAWAY/KEY POINTS:

Fluoxetine has the longest half-life at 4-6 days compared to other SSRIs. For this reason, it carries the lowest risk of discontinuation symptoms and can be tapered the fastest upon discontinuation.

REFERENCE:

[1] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.
[2] VandenBerg AM. Depressive Disorders. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey LM, eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

The correct answer is: Fluoxetine

Question 3
ID: 50276
Correct
Flag question

A physician from your community is calling to discuss the care plan for a mutual patient, FL, who is a 30-year-old female diagnosed with Major Depressive Disorder (MDD) 1 year ago. When she was diagnosed, she began a trial of sertraline 100 mg PO daily, which she is still currently taking. The patient reports that her depression has somewhat improved, however, she has had complaints of weight gain and difficulty sleeping since starting sertraline. The physician has informed you that after their appointment today, the decision has been made to switch FL to venlafaxine 75 mg PO daily. He

is now seeking your recommendation on how to approach this.

Which of the following options is the most appropriate plan for switching antidepressants?

Select one:

- Start low-dose venlafaxine now, slowly increasing to the target dose as you taper down sertraline to eventually stop it ✔

  Rose Wang (ID:113212) this answer is correct. A cross-taper taper is the most appropriate method of switching from sertraline to venlafaxine given the patient's current dose.

- Start low-dose venlafaxine now, slowly increasing to the target dose, then taper and stop sertraline ✖
- Taper and stop sertraline, wait 1 week, then start low-dose venlafaxine, slowly increasing to the target dose ✖
- Stop sertraline now, then start low-dose venlafaxine, slowly increasing to the target dose ✖

Correct

Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Understand how to switch between antidepressants safely and effectively.

BACKGROUND:

The onset of therapeutic effects for antidepressants is usually 2-4 weeks. Improvement is defined as a 20 to 30% or greater reduction in symptoms after 2-4 weeks of therapy, where improvement is assessed using a validated depression rating scale. In the case of no improvement at maximally tolerated doses, the antidepressant should be switched to another first-line antidepressant with superior efficacy. Alternatively, adding-on therapy can be considered. This is described as augmentation therapy and the first-line adjunctive agents that have shown superior efficacy include aripiprazole, quetiapine, and risperidone. Symptom remission should be assessed after 8-12 weeks of treatment. If symptoms have not resolved, switching antidepressants or adding-on a medication, as described above, should be considered. If more than one first-line agent with superior efficacy has failed, then the antidepressant can be switched to a second- or third-line agent or rTMS can be considered. Treatment-resistant depression is commonly defined as an inadequate response to 2 or more antidepressants. Ketamine and esketamine, NMDA receptor antagonists, are increasingly being investigated for their rapid effects in treatment-resistant depression. Once symptom remission is achieved, the antidepressant treatment should be maintained for 6 to 9 months, or for at least 2 years in some cases, to reduce relapse rates. Longer maintenance treatment of 2 years or more is recommended if the following risk factors for recurrence are present: psychiatric comorbidities, frequent and recurrent episodes (3 or more), residual symptoms (lack of remission), severe episodes (ie. suicidality), or difficult-to-treat or chronic episodes. Serotonin syndrome is a rare, serious adverse event that can be described by the mnemonic SHIVERS, which may include shivering, hyperreflexia (overactive reflexes), increased temperature, unstable vital signs (increased heart rate and respiratory rate and low blood pressure), encephalopathy, restlessness, and sweating. These symptoms can arise when there is too much serotonin in the body and this usually occurs when multiple serotonergic agents are being used at the same time. If serotonin syndrome is suspected, the precipitating medication should be stopped and the patient should be referred to the hospital. A washout period may be required, depending on the half-life of the first antidepressant agent. Irreversible Monoamine Oxidase Inhibitors (MAOIs) have the highest risk of serotonin syndrome and require a minimum 2-week washout period when switching to another antidepressant. Moclobemide requires a 5-day washout period when switching to another serotonergic agent. When switching from any other antidepressant to an irreversible MAOI, a washout period of 5 half-lives of the first antidepressant is recommended. Additionally, fluoxetine requires a 5-week washout period when being switched to an irreversible MAOI, due to its long half-life. Otherwise, when switching between most other antidepressants (i.e. Selective Serotonin Reuptake Inhibitors (SSRIs) excluding fluoxetine, and Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)), a washout period is not required, and a cross-tapering technique can be applied with careful monitoring for serotonin syndrome. Withdrawal symptoms can be described by the FINISH mnemonic and include flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal. These unpleasant, but non life-threatening symptoms may be experienced by up to 40% of patients when antidepressants are stopped abruptly. Therefore, when discontinuing antidepressants, taper slowly over 4 to 6 weeks to prevent withdrawal symptoms. Patients are at risk if they have been using the antidepressants for a minimum of 6 weeks. Paroxetine and venlafaxine are the most likely to be associated with discontinuation symptoms; whereas, fluoxetine and vortioxetine cause little to no withdrawal symptoms.

RATIONALE:

Correct Answer:

- **Start low-dose venlafaxine now, slowly increasing to the target dose as you taper down sertraline to eventually stop it** - A cross-taper taper is the most appropriate method of switching from sertraline to venlafaxine given the patient's current dose.

Incorrect Answers:

- **Start low-dose venlafaxine now, slowly increasing to the target dose, then taper and stop sertraline** - Sertraline should be tapered down as venlafaxine is tapered up (cross-taper).
- **Taper and stop sertraline, wait 1 week, then start low-dose venlafaxine, slowly increasing to the target dose** - A washout period of 1 week is not necessary when stopping sertraline.
- **Stop sertraline now, then start low-dose venlafaxine, slowly increasing to the target dose** - Sertraline should be tapered down before stopping to minimize the risk of discontinuation symptoms.

TAKEAWAY/KEY POINTS:

In cases of unresolved symptoms or adverse effects, patients may consider switching their antidepressant therapy. In most cases, a washout period is not required, and a cross-tapering technique can be applied with careful monitoring for serotonin syndrome. Certain medications, such as MAOIs, moclobemide, and fluoxetine, require more strict switching techniques involving longer washout periods.

REFERENCE:

[1] Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments. *Can J Psychiatry*. 2016;61(9):540-560. doi:10.1177/0706743716659417. [2] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.

The correct answer is: Start low-dose venlafaxine now, slowly increasing to the target dose as you taper down sertraline to eventually stop it

Question 4

ID: 50280

Correct

Flag question

Send Feedback

A medical resident who works in a mental health clinic is monitoring a mutual patient as he tapers off his antidepressant. The patient is HT, a 42-year-old male who has been on paroxetine 40 mg PO daily for the last 10 months for depression and is now in remission. HT did not present with any risk factors that indicated the team to consider longer-term (i.e. 2 years or longer) treatment maintenance. HT has had no complaints of adverse effects and reports that his mood has improved greatly. The medical resident has informed you that they plan to taper off paroxetine over a period of 4-6 weeks. HT reported that he is looking forward to stopping this medication, and is eager to do so as quickly as possible.

All of the following are important to provide to the medical resident regarding antidepressant discontinuation **EXCEPT:**

Select one:

- HT should be counselled on the common symptoms of antidepressant withdrawal, including flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal ✖
- Paroxetine has a short half-life and is less likely to result in withdrawal symptoms compared to other antidepressants ✔

  Rose Wang (ID:113212) this answer is correct. Antidepressants with shorter half-lives (e.g. paroxetine and venlafaxine) are more likely to cause withdrawal symptoms.
- If HT experiences withdrawal symptoms, paroxetine can be reintroduced and tapered more slowly ✖
- Withdrawal symptoms can begin within 1 week of stopping an antidepressant and typically last for 3 days to 3 weeks ✖

Correct

Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Understand the important considerations regarding antidepressant discontinuation.

BACKGROUND:

Antidepressant discontinuation syndrome occurs when a patient has been consistently taking an antidepressant (e.g. selective serotonin reuptake inhibitors, selective serotonin & norepinephrine reuptake inhibitors, tricyclic antidepressants etc.) and stops the drug abruptly or tapers down too fast. The risk occurs when a patient has been taking an antidepressant for 6 weeks or longer. Withdrawal symptoms can be described by the FINISH mnemonic and include flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal. These unpleasant, but non life-threatening symptoms may be experienced by up to 40% of patients when antidepressants are stopped abruptly. Therefore, when discontinuing antidepressants, taper slowly over 4 to 6 weeks to prevent withdrawal symptoms. Patients are at risk if they have been using the antidepressants for a minimum of 6 weeks. Paroxetine and venlafaxine are the most likely to be associated with discontinuation symptoms; whereas, fluoxetine and vortioxetine cause little to no withdrawal symptoms. Side effects of Selective Serotonin Reuptake Inhibitors (SSRIs) include insomnia (especially fluoxetine and sertraline which are more activating) or drowsiness, sexual dysfunction and Gastrointestinal (GI) upset. The CNS and GI side effects normally subside within 2 weeks; however, sexual dysfunction could persist for the duration of treatment. Additionally, when initiating an SSRI or increasing the dose, anxiety and agitation are common side effects that may occur; however, they usually subside within a few weeks. SSRIs can increase the risk of GI bleeding and should be used with caution in individuals at higher risk of GI bleeding (such as concomitant NSAID use). In addition, fluoxetine has a uniquely long half-life of 4-6 days (9 days for active metabolite norfluoxetine), allowing for faster tapering upon discontinuation compared to other SSRIs. A meta-analysis comparing escitalopram to citalopram found that escitalopram, the stereoisomer of citalopram, was superior in efficacy, but comparable in adverse events to citalopram. Both citalopram and escitalopram carry the greatest risk amongst the SSRIs of prolongation of QTc. In addition, paroxetine has the greatest anticholinergic effects and causes the greatest amount of weight gain among the SSRI drug class.

RATIONALE:

Correct Answer:

- **Paroxetine has a short half-life and is less likely to result in withdrawal symptoms compared to other antidepressants** - Antidepressants with shorter half-lives (e.g. paroxetine and venlafaxine) are more likely to cause withdrawal symptoms

more likely to cause withdrawal symptoms.

Incorrect Answers:

- **HT should be counselled on the common symptoms of antidepressant withdrawal, including flu-like symptoms, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal** - These are common symptoms to monitor for in antidepressant withdrawal and can be described by the FINISH mnemonic.
- **If HT experiences withdrawal symptoms, paroxetine can be reintroduced and tapered more slowly** - This is an appropriate strategy for managing antidepressant discontinuation symptoms.
- **Withdrawal symptoms can begin within 1 week of stopping an antidepressant and typically last for 3 days to 3 weeks** - Withdrawal symptoms typically begin 1-7 days after stopping an antidepressant and most often last for 3 days to 3 weeks, but in some cases, may persist for several months.

TAKEAWAY/KEY POINTS:

Certain antidepressants such as paroxetine and venlafaxine carry a greater risk of withdrawal symptoms, but patients should always monitor for these symptoms (described by the FINISH mnemonic), during the appropriate timeframe when discontinuing. A slow taper over 4-6 weeks is typically sufficient to prevent experiencing withdrawal symptoms but, if necessary, the antidepressant can be reintroduced and tapered more slowly to better manage these symptoms.

REFERENCE:

[1] Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments. Can J Psychiatry. 2016;61(9):540-560. doi:10.1177/0706743716659417.
[2] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.
[3] Warner CH, Bobo W, Warner C, Reid S, Rachal J. Antidepressant discontinuation syndrome. *Am Fam Physician*. 2006;74(3):449-456.

The correct answer is: Paroxetine has a short half-life and is less likely to result in withdrawal symptoms compared to other antidepressants

Question 5

ID: 50284

Correct

Flag question

Send Feedback

RR, a 68-year-old female, is seeking your advice for her newly diagnosed mild Major Depressive Disorder (MDD). She expresses concerns about taking prescription medications and inquires about alternative treatment options. She has no medication allergies, and currently takes tiotropium 2.5 mcg/puff 2 puffs daily for her Chronic Obstructive Pulmonary Disease (COPD).

You recommend all of the following alternative treatment options as first-line monotherapy for the management of Major Depressive Disorder (MDD) **EXCEPT**:

Select one:

a. St. John's wort ✖

b. Physical exercise ✖

c. Omega-3 fatty acids ✔

Rose Wang (ID:113212) this answer is correct. Omega-3 fatty acids are considered second-line as monotherapy for mild-moderate depression due to the conflicting body of evidence.

d. Psychotherapy ✖

Correct

Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Understand the efficacy and place in therapy of alternative treatment options for the treatment of MDD.

BACKGROUND:

Major Depressive Disorder (MDD) is a mental health disorder characterized by a state of low/depressed mood which impacts an individual's emotional, physical, cognitive, and behavioural well-being. MDD is diagnosed using the DSM-5 criteria which identify symptoms such as appetite changes, sleep changes, depressed mood, loss of pleasure and their impact on a person's functionality. Non-pharmacologic and pharmacologic therapy is the mainstay of treatment. While various antidepressants have been developed and tested to treat MDD, some patients will choose to try alternative treatment options. It is therefore important to know the evidence available behind the safety and efficacy of such treatment options. In patients with mild to moderate depression, St. John's Wort has evidence to support its use as a first-line agent. It is important to counsel patients that this drug has many drug interactions as it is a strong CYP 3A4 inducer. Furthermore, there is a risk for serotonin syndrome if St. John's Wort is combined with other drugs that have serotonergic properties. Regular physical exercise is recommended as first-line monotherapy for mild-to-moderate depression and as an adjunct to pharmacotherapy and/or psychotherapy in moderate to severe depression. The recommended amount of exercise is at least 30 minutes of moderate-intensity exercise, either aerobic or resistance type, at least three times weekly for a minimum of 9 weeks. Omega-3 fatty acids have conflicting evidence to support their use and are thereby considered second-line as monotherapy for mild to moderate depression or as an adjunctive therapy for moderate to severe depression. Drugs such as bupropion, citalopram and sertraline are considered first-line options in depression too.

RATIONALE:

Correct Answer:

- **Omega-3 fatty acids** - Omega-3 fatty acids are considered second-line as monotherapy for mild-moderate depression due to the conflicting body of evidence.

Incorrect Answers:

- **St. John's wort** - St. John's wort is effective as first-line monotherapy in mild-moderate MDD.
- **Physical exercise** - Physical exercise is effective as first-line monotherapy in mild-moderate depression.
- **Psychotherapy** - Psychotherapy is considered to be as effective as medications in mild-moderate depression.

TAKEAWAY/KEY POINTS:

There are a number of alternative treatment options that patients may enquire about for MDD including natural health products, neurostimulation, and other non-pharmacologic treatments. It is important to understand the available evidence behind the safety and efficacy of such treatment options to make the most appropriate recommendation. St. John's wort, physical exercise, and psychotherapy are examples of such options that can be recommended as first-line monotherapy for MDD, in appropriate situations.

REFERENCE:

[1] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices, Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.
[2] Ravindran A, Balneaves L, Faulkner G et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder. *The Canadian Journal of Psychiatry*. 2016;61(9):576-587. doi:10.1177/0706743716660290

The correct answer is: Omega-3 fatty acids

Question 6

ID: 50285

Correct

Flag question

Send Feedback

PD is a 32-year-old male patient who was recently diagnosed with Major Depressive Disorder (MDD). He has an allergy to sulfa medications and his medical history includes Type 2 Diabetes Mellitus (T2DM), which has been well-controlled on metformin 500 mg PO BID for 6 years, and Gastroesophageal Reflux Disease (GERD), which he manages with pantoprazole 40 mg PO daily since last year. PD has agreed to start a trial of antidepressant therapy. He is currently overweight (BMI 27 kg/m^2). PD heard from his friends that antidepressants can cause weight gain and sexual dysfunction, and he informs you that these are side effects that he is very concerned about.

Which of the following antidepressants would be the most appropriate to recommend for PD?

Select one:

a. Mirtazapine ✗

b. Clomipramine ✗

c. Nortriptyline ✓

Rose Wang (ID:113212) this answer is correct. Nortriptyline is a secondary amine tricyclic antidepressant (TCA) and is associated with less weight gain and sexual dysfunction compared to the other options.

d. Paroxetine ✗

Correct

Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Understand the side effects of treatment options for Major Depressive Disorder (MDD).

BACKGROUND:

Pharmacological treatments are generally recommended for moderate to severe depression and may also be considered in mild depression. First-line therapies for depression include Selective Serotonin reuptake inhibitors (SSRIs), Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), bupropion, mirtazapine, and vortioxetine. The first-line SSRIs include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, and the first-line SNRIs include desvenlafaxine, duloxetine, venlafaxine. A network meta-analysis of 21 antidepressants found escitalopram, sertraline, mirtazapine, and venlafaxine to be superior in efficacy for the treatment of depression. St. John's Wort is a natural health product that is also a first-line agent if MDD is mild to moderate in severity and after potential drug interactions have been considered. There are a number of drug interactions that exist with St. John's Wort as it is a potent inducer of CYP3A4 and P-glycoprotein.

RATIONALE:

Correct Answer:

- **Nortriptyline** - Nortriptyline is a secondary amine tricyclic antidepressant (TCA) and is associated with less weight gain and sexual dysfunction compared to the other options.

Incorrect Answers:

- **Mirtazapine** - Mirtazapine is a dual-action antidepressant (norepinephrine and serotonin) and is

associated with weight gain.

- **Clomipramine** - Clomipramine is a tertiary amine tricyclic antidepressant (TCA) and is associated with weight gain and sexual dysfunction.
- **Paroxetine** - Paroxetine is a selective serotonin reuptake inhibitor (SSRI) and is associated with weight gain and sexual dysfunction.

TAKEAWAY/KEY POINTS:

Understanding the differences in side effect profiles for available treatment options in MDD is important when recommending the most appropriate medication for a patient based on their preferences and comorbid conditions. Secondary amine TCAs are better tolerated than tertiary amine TCAs.

REFERENCE:

[1] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices, Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.

[2] Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments. The Canadian Journal of Psychiatry. 2016;61(9):540-560. doi:10.1177/0706743716659417

The correct answer is: Nortriptyline

Question 7

ID: 50286

Correct

Flag question

Send Feedback

According to the clinical guidelines, all of the following are indications that support the long-term (i.e. 2 years or longer) use of antidepressants, **EXCEPT:**

Select one:

- Family history of mental health disorders ✔ *Rose Wang (ID:113212) this answer is correct. This is not an indication that supports long-term therapy.*
- Frequent and recurrent episodes of depression ✖
- Psychotic features in depressive episodes ✖
- Significant medical comorbidities ✖

Correct

Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Recognize indications for long-term use of antidepressants.

BACKGROUND:

Major Depressive Disorder (MDD) is a mental health disorder characterized by a state of low/depressed mood which impacts an individual's emotional, physical, cognitive, and behavioural well-being. MDD is diagnosed using the DSM-5 criteria which identify symptoms such as appetite changes, sleep changes, depressed mood, loss of pleasure and their impact on a person's functionality. Non-pharmacologic and pharmacologic therapy is the mainstay of treatment. Once pharmacologic therapy is started, patients should be monitored for side effects of the antidepressant, improvement in their emotional and physical symptoms, and improvement in their functionality. Antidepressants should be used for 6-9 months after full symptom remission for the first episode. For patients with a history of >2 depressive episodes, therapy should be continued for at least 2 years. Other indications for long-term use of antidepressants include: older age, psychotic features, suicidality, frequent episodes, residual symptoms, difficult-to-treat episodes, and comorbid psychiatric or medical conditions. These factors can increase a patient's risk for relapse and thus it is recommended for patients in these scenarios to be on antidepressants for a longer duration.

RATIONALE:

Correct Answer:

- **Family history of mental health disorders** - This is not an indication that supports long-term therapy.

Incorrect Answers:

- **Frequent and recurrent episodes of depression** - This is an indication that supports long-term anti-depressant therapy.
- **Psychotic features in depressive episodes** - Severe depressive episodes, including the presence of psychosis, is an indication that supports long-term anti-depressant therapy.
- **Significant medical comorbidities** - This is an indication that supports long-term anti-depressant therapy.

TAKEAWAY/KEY POINTS:

Factors that can increase a patient's risk for relapse, including frequent and recurrent symptoms, psychotic features, and significant comorbidities, may warrant the use of long-term treatment (i.e. at least 2 years). Family history is not included as one of these risk factors in the CANMAT guidelines.

REFERENCE:

[1] Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT)

2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments. Can J Psychiatry. 2016;61(9):540-560. doi:10.1177/0706743716659417.
[2] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices, Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.

The correct answer is: Family history of mental health disorders

Question 8
ID: 50287
Correct
Flag question
Send Feedback

JD is a 48-year-old female who is a high school teacher and the mother of two teenagers. She was diagnosed with MDD 10 years ago and is currently being treated for treatment-resistant depression. She comes to you today with new onset of restlessness, shivering, and sweating. Her children also told her she seemed "off" recently. She has no allergies and no other medical conditions.

Her current medications include the following:

- **Fluoxetine 80 mg PO daily x 2 years**
- **Quetiapine 50 mg PO daily x 3 months**
- **St. John's wort 300 mg PO TID x 1 week**

Which of the following statements is the most likely explanation for JD's symptoms?

Select one:

a. JD is experiencing a symptom of chronic severe treatment-resistant depression and requires a change in antidepressant therapy ✖

b. JD is experiencing a side effect of the St. John's wort, which will subside with time ✖

c. JD is experiencing serotonin syndrome and must be referred to the emergency department ✔

Rose Wang (ID:113212) this answer is correct. JD is on multiple serotonergic medications and experiencing classic symptoms of serotonin syndrome, which requires immediate medical attention.

d. JD is experiencing a drug interaction between St. John's wort and quetiapine and requires a dose reduction ✖

Correct
Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Understand how to recognize the symptoms and risk factors of serotonin syndrome.

BACKGROUND:

Depression is a complex mood disorder that can greatly affect patients' mental and physical well-being. Depressive disorders include Major Depressive Disorder (MDD), Persistent Depressive Disorder (PDD), or dysthymia, disruptive mood dysregulation disorder, premenstrual dysphoric disorder, substance/medication-induced disorder, depressive disorder due to a general medical condition, other specified depressive disorder (where the episodes deviate from the precise criteria for MDD), and unspecified depressive disorder. All these disorders have the common features of sad, empty or irritable mood that affect the individual's ability to function. MDD will be the primary focus. The pathophysiology of depression remains unclear. There are many possible causes of depression, such as family history, brain chemistry and major stressful life events. Twin studies have demonstrated the influence genetics has on developing depression and have revealed a higher risk of depression in women compared to men. Environmental factors, such as childhood trauma and poor social support, are equally important in contributing to the development of depression. One of the early biological hypotheses suggested that depression was due to the decreased levels and functioning of the monoamine neurotransmitters (NTs), serotonin, norepinephrine, dopamine, gamma aminobutyric acid (GABA), and glutamate neurotransmitters in the brain. Most antidepressants work by blocking the transporter molecules, thereby inhibiting the reuptake of NTs and increasing their levels in the synapse. This reuptake inhibition occurs immediately after administration of an antidepressant; however, therapeutic effects usually begin after 2 to 4 weeks. Pharmacological treatments are generally recommended for moderate to severe depression and may also be considered in mild depression. First-line therapies for depression include Selective Serotonin reuptake inhibitors (SSRIs), Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), bupropion, mirtazapine, and vortioxetine. The first-line SSRIs include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, and the first-line SNRIs include desvenlafaxine, duloxetine, venlafaxine. A network meta-analysis of 21 antidepressants found escitalopram, sertraline, mirtazapine, and venlafaxine to be superior in efficacy for the treatment of depression. St. John's Wort is a natural health product that is also a first-line agent if MDD is mild to moderate in severity and after potential drug interactions have been considered. There are a number of drug interactions that exist with St. John's Wort as it is a potent inducer of CYP3A4 and P-glycoprotein. Serotonin syndrome is a rare, serious adverse event that can be described by the mnemonic SHIVERS, which may include shivering, hyperreflexia (overactive reflexes), increased temperature, unstable vital signs (increased heart rate and respiratory rate and low blood pressure), encephalopathy, restlessness, and sweating. These symptoms can arise when there is too much serotonin in the body and this usually occurs when multiple serotonergic agents are being used at the same time. If serotonin syndrome is suspected, the precipitating medication should be stopped and the patient should be referred to the hospital. Irreversible MAOIs have the highest risk of serotonin syndrome and require a minimum 2-week washout period when switching to another antidepressant. Moclobemide requires a 5-day washout period when switching to another serotonergic agent. When switching from any other antidepressant to an irreversible MAOI, a washout period of 5 half-lives of the first antidepressant is recommended. Additionally, fluoxetine requires a 5-week washout period when being switched to an irreversible MAOI, due to its long half-life. Otherwise, when switching between most other antidepressants, a washout period is not required, and a cross-tapering technique can be applied with careful monitoring for serotonin syndrome.

RATIONALE:

Correct Answer:

- **JD is experiencing serotonin syndrome and must be referred to the emergency department** - JD is on multiple serotonergic medications and experiencing classic symptoms of serotonin syndrome, which requires immediate medical attention.

Incorrect Answers:

- **JD is experiencing a symptom of chronic severe treatment-resistant depression and requires a change in antidepressant therapy** - Her symptoms are acute and not likely related to her treatment-resistant depression.
- **JD is experiencing a side effect of the St. John's wort, which will subside with time** - Although she may be experiencing side effects of St. John's wort, it is more likely due to a drug interaction and it is not appropriate to continue the medication.
- **JD is experiencing a drug interaction between St. John's wort and quetiapine and requires a dose reduction** - A drug interaction is likely the cause, however, a dose reduction is not the most appropriate solution.

TAKEAWAY/KEY POINTS:

Serotonin syndrome is a rare but serious adverse event which must be monitored for in patients on multiple serotonergic agents. If present, it requires stopping the offending agent and ensuring the patient seeks immediate medical attention.

REFERENCE:

[1] Kennedy SH, Lam RW, McIntyre RS, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 3. Pharmacological Treatments. *Can J Psychiatry*. 2016;61(9):540-560. doi:10.1177/0706743716659417.
[2] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.
[3] VandenBerg AM. Depressive Disorders. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey LM, eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

The correct answer is: JD is experiencing serotonin syndrome and must be referred to the emergency department

Question 9
ID: 50307
Incorrect
Flag question
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GC is a married 57-year-old male accountant who was recently started on citalopram 10 mg PO daily for depression. He has no known allergies. He has fibromyalgia which was diagnosed last year. GC is also a regular smoker with a 20 pack-year history. His current medications include the following:

- **Cyclobenzaprine 10 mg PO QHS x 1 year**
- **Ibuprofen 400 mg PO PRN x 2 years**
- **Men's Multivitamin + Minerals PO daily x 7 years**

All of the following are important counselling points for GC **EXCEPT:**

Select one:

a. Advise GC to switch ibuprofen to acetaminophen due to an increased risk of gastrointestinal bleeding with concomitant citalopram and ibuprofen use ✖

b. Sexual dysfunction is a known side effect of citalopram which may persist for the duration of treatment ✖

Rose Wang (ID: 113212) this answer is incorrect. SSRIs are strongly associated with sexual dysfunction, especially when compared to other antidepressant classes. Unlike some other side effects, this does not often subside over time.

c. Always consult a health care provider before starting a new over-the-counter (OTC) medication to assess for an interaction that may increase the risk of serotonin syndrome ✖

d. Offer to contact GC's physician to switch antidepressants due to the risk of lowered seizure threshold with concomitant citalopram and cyclobenzaprine use ✔

Incorrect
Marks for this submission: 0.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Identify the important adverse effects and drug interactions of SSRI therapy.

BACKGROUND:

Side effects of Selective Serotonin Reuptake Inhibitors (SSRIs) include insomnia (especially fluoxetine and sertraline which are more activating) or drowsiness, sexual dysfunction and Gastrointestinal (GI) upset. The CNS and GI side effects normally subside within 2 weeks; however, sexual dysfunction could persist for the duration of treatment. Additionally, when initiating an SSRI or increasing the dose, anxiety and agitation are common side effects that may occur; however, they usually subside within a few weeks. SSRIs can increase the risk of GI bleeding and should be used with caution in individuals at higher risk of GI bleeding (such as concomitant NSAID use). In addition, fluoxetine has a uniquely long half-life of 4-6 days (9 days for active metabolite norfluoxetine), allowing for faster tapering upon discontinuation compared to other SSRIs. A meta-analysis comparing escitalopram to citalopram found that escitalopram, the stereoisomer of citalopram, was superior in efficacy, but comparable in adverse events to citalopram. Both citalopram and escitalopram carry the greatest risk amongst the SSRIs of prolongation of QTc. In addition, paroxetine has the greatest anticholinergic effects and causes the greatest amount of weight gain among the SSRI drug class. Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) are also first-line agents for depression and have some notable side effects compared to the SSRIs. All SNRIs may be associated with increased blood pressure and

heart rate; therefore, these vital signs should be monitored prior to and during therapy. Dose-related hypertension may occur with doses of 225 mg or more daily of venlafaxine. Similarly, duloxetine has a risk of hypertension at higher doses of 120 mg/day. In addition to depression, duloxetine is used to treat neuropathic pain and fibromyalgia and may be beneficial if a patient with depression has these concomitant disorders. The newer agent, levomilnacipran, uniquely has more selectivity for norepinephrine than serotonin reuptake inhibition (2:1) compared to other SNRIs. Levomilnacipran is currently a second-line agent as there are fewer comparison studies to date and it is the most costly of the SNRI class. Moreover, desvenlafaxine is one of the few antidepressants that was evaluated and found to be effective in peri- and post-menopausal women. Bupropion is a first-line antidepressant and is also indicated for smoking cessation. Bupropion lowers the seizure threshold; therefore, it is contraindicated in patients with a seizure disorder, a recent history of anorexia or bulimia nervosa, severe head trauma, an electrolyte disorder, and in patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs. It should be used with caution with alcohol and other medications that reduce the seizure threshold, such as meperidine, tramadol, TCAs and theophylline. Compared to SSRIs, sexual dysfunction occurs less frequently with bupropion. Similarly, mirtazapine has low rates of sexual side effects and may be considered; although, mirtazapine is greatly associated with sedation and weight gain. Serotonin syndrome is a rare, serious adverse event that can be described by the mnemonic SHIVERS, which may include shivering, hyperreflexia (overactive reflexes), increased temperature, unstable vital signs (increased heart rate and respiratory rate and low blood pressure), encephalopathy, restlessness, and sweating. These symptoms can arise when there is too much serotonin in the body and this usually occurs when multiple serotonergic agents are being used at the same time. If serotonin syndrome is suspected, the precipitating medication should be stopped and the patient should be referred to the hospital.

RATIONALE:

Correct Answer:

- **Offer to contact GC's physician to switch antidepressants due to the risk of lowered seizure threshold with concomitant citalopram and cyclobenzaprine use** - Lowered seizure threshold is not a known side effect of citalopram, so this interaction is not an important concern for GC.

Incorrect Answers:

- **Advise GC to switch ibuprofen to acetaminophen due to an increased risk of gastrointestinal bleeding with concomitant citalopram and ibuprofen use** - SSRIs can increase the risk of gastrointestinal bleeding and should be used with caution in patients at higher risk (e.g. concomitant NSAID use).
- **Sexual dysfunction is a known side effect of citalopram which may persist for the duration of treatment** - SSRIs have a high incidence of causing sexual dysfunction, especially when compared to other antidepressant classes. Unlike some other side effects, this does not often subside over time.
- **Always consult a health care provider before starting a new over-the-counter (OTC) medication to assess for an interaction that may increase the risk of serotonin syndrome** - Serotonin syndrome can occur when multiple serotonergic agents are used concomitantly (including SSRIs). Some common OTC products can be involved in this interaction.

TAKEAWAY/KEY POINTS:

Serotonin syndrome, sexual dysfunction, and GI bleeding are possible adverse effects and important interaction risks associated with SSRIs.

REFERENCE:

[1] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.
[2] VandenBerg AM. Depressive Disorders. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey LM, eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

The correct answer is: Offer to contact GC's physician to switch antidepressants due to the risk of lowered seizure threshold with concomitant citalopram and cyclobenzaprine use

Question 10
ID: 50310
Correct
Flag question
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You are providing a follow-up consultation with a 42-year-old patient, LM, who has been dealing with Major Depressive Disorder (MDD) for several months. LM has been taking sertraline 50 mg PO daily for the past eight weeks, but he reports experiencing only minimal improvement in his depressive symptoms. Specifically, he estimates around 15% improvement in his condition since initiating sertraline. While he has encountered mild gastrointestinal discomfort as an adverse effect, he deems it manageable. This is LM's first medication trial for his MDD.

Which of the following treatment approaches would be the most appropriate recommendation for LM?

Select one:

- Consider switching to a different antidepressant ✔

Rose Wang (ID:113212) this answer is correct. Switching antidepressants is appropriate due to LM's minimal response to sertraline and as this is his first antidepressant trial.

- Continue sertraline and monitor for further improvement ✖
- Consider discontinuation of sertraline ✖
- Consider adding an adjunctive medication ✖

Correct
Marks for this submission: 1.00/1.00.

TOPIC: Depression

LEARNING OBJECTIVE:

Determine which clinical factors impact the decision to switch to another antidepressant or add an adjunctive medication.

BACKGROUND:

The onset of therapeutic effects for antidepressants is usually 2-4 weeks. Improvement is defined as a 20 to 30% or greater reduction in symptoms after 2-4 weeks of therapy, where improvement is assessed using a validated depression rating scale. In the case of no improvement at maximally tolerated doses, the antidepressant should be switched to another first-line antidepressant with superior efficacy. Alternatively, adding-on therapy can be considered. This is described as augmentation therapy and the first-line adjunctive agents that have shown superior efficacy include aripiprazole, quetiapine, and risperidone.

Clinical factors that would favour switching to a different monotherapy antidepressant include: the first antidepressant trial, adverse effects that are difficult to tolerate, <25% improvement in condition, less severe symptoms or impairment, or the patient's choice.

Alternatively, clinical factors that would favour adding an adjunctive medication include: the patient has already tried 2 or more antidepressants, inability to manage current adverse effects, >25% improvement in condition, more severe symptoms or more functional impairment, and the patient's choice.

RATIONALE:

Correct Answer:

- **Consider switching to a different antidepressant** - Switching antidepressants is appropriate due to LM's minimal response to sertraline and as this is his first antidepressant trial.

Incorrect Answers:

- **Continue sertraline and monitor for further improvement** - Continuing with sertraline is not the best option given LM's minimal improvement.
- **Consider discontinuation of sertraline** - Complete discontinuation of antidepressant therapy would not be advisable as LM's symptoms persist and warrant further treatment.
- **Consider adding an adjunctive medication** - Augmentation may be considered, but switching to a different antidepressant is a more suitable initial step based on LM's clinical factors.

TAKEAWAY/KEY POINTS:

There are certain clinical factors that must be considered when deciding to switch therapy or augment therapy including the number of antidepressant trials, tolerability of adverse effects, improvement in condition, severity of symptoms, and the patient's choice.

REFERENCE:

[1] Kennedy SH, Parikh SV, and Grigoriadis S. Depression. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.
[2] VandenBerg AM. Depressive Disorders. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey LM, eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

The correct answer is: Consider switching to a different antidepressant

Finish review